

## AMENDMENT

### In the Claims

Please cancel claims 1-12 and 29-32, withdraw claims 13-28 and 33-60, and add new claims 61-76 as follows.

61. (New) An isolated nucleic acid encoding a 3-OST protein, wherein the nucleic acid encodes a 3-O-sulfotransferase domain of a 3-OST-1 protein.

62. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid encodes a 3-OST protein comprising a mature human 3-OST-1 protein.

63. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid encodes a 3-OST protein comprising a mature murine 3-OST-1 protein.

64. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1.

65. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises a sequence having at least 85% nucleotide sequence identity with SEQ ID NO: 1 and encodes a functional fragment having sequence-specific HS binding affinity.

66. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises a nucleotide sequence encoding residues 21-307 of SEQ ID NO: 2.

67. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises a nucleotide sequence encoding residues 53-311 of SEQ ID NO 2.

68. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises a nucleotide sequence encoding residues 250-276 of SEQ ID NO 2 encoding a functional fragment having

specific HS binding affinity.

69. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 3.

70. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises a nucleotide sequence encoding residues 21-303 of SEQ ID NO: 4.

71. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises a nucleotide sequence encoding residues 49-307 of SEQ ID NO 4.

72. (New) The isolated nucleic acid of claim 61 wherein the nucleic acid comprises a nucleotide sequence encoding residues 246-272 of SEQ ID NO 4 and encoding a functional fragment having specific HS binding affinity.

73. (New) A host cell transformed with a nucleic acid of any one of claims 61-72 or a descendant thereof.

74. (New) The host cell of claim 73 wherein the host cell is selected from the group consisting of bacterial cells, yeast cells, and insect cells.

75. (New) The host cell of claim 73 wherein the cell is a mammalian cell.

76. (New) The host cell of claim 73 wherein the cell is selected from the group consisting of COS-7 cells, CHO cells, murine primary cardiac microvascular endothelial cells (CME), murine mast cell line C57.1, human primary endothelial cells of umbilical vein (HUVEC), F9 embryonal carcinoma cells, rat fat pad endothelial cells (RFPEC), and L cells.

## RESPONSE

Claims 1-60 were pending in the Application. In a Response to Restriction Requirement earlier filed on August 16, 2001, Applicants elected, with traverse, to pursue prosecution of Group I, claims 1-12 and 29-32 drawn to isolated nucleic acids encoding a full length or fragments of 3-OST protein. Applicants hereby affirm the election with traverse of Group I (nucleic acids and host cells encoding 3-OST-1).

Claims 1-12 and 29-32 are cancelled, claims 13-28 and 33-60 are withdrawn, and claims 61-76 are added by the present Amendment. New claims 61-76 are directed to the subject matter of Group I. Upon entry of the present Amendment, claims 61-76 are pending and presented for consideration.

Support for new claims 61-76 may be found throughout the specification at, for example, page 11, line 19 through page 12, line 25, and in originally-filed claims 1-12 and 29-32.

Applicants respectfully submit that no new matter is introduced by the present Amendment.

### **Oath/Declaration**

Applicants acknowledge that the Declaration was objected to as not referencing priority to PCT/US98/22597 under 35 USC §120. Applicants will submit a Substitute Declaration in due course.

### **Rejections Under 35 U.S.C. §112, First Paragraph**

*Claims 29-32 -- 35 U.S.C. §112, first paragraph*

Claims 29-32 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In order to expedite prosecution of the inventive nucleic acids, claims 29-32 have been cancelled without prejudice and none of the new claims presented herewith are

directed to transgenic animals. Accordingly, Applicants submit that 35 U.S.C § 112, first paragraph rejection of claims 29-32 is rendered moot.

*Claims 1, 5, 6, and 8-12 -- 35 U.S.C. §112, first paragraph*

Claims 1, 5, 6, and 8-12 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The fundamental factual inquiry in a written description rejection is whether the claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement. MPEP 2163.02. The Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257, 265, 191 USPQ 90, 98 (CCPA 1976); *Ex parte Sorenson*, 3 USPQ2d 1462, 1463 (BPAI 1987). MPEP 2163.04.

Independent claim 1 is directed to a nucleic acid encoding a 3-OST-1 protein. The instant application describes two 3-OST-1 proteins using complete nucleotide sequences. Furthermore, Applicants have clearly identified and properly described multiple 3-OST-1 domains and their characteristic functions.

After the 3-OST-1 signal peptide, there is a domain rich in the residues S, P, L, A, and G (SPLAG-rich domain) (residues 21-52 of SEQ ID NO: 2 and residues 21-48 of SEQ ID NO: 4). (See page 12, lines 5-7.)

Thus, Applicants teach that residues 21-52 of SEQ ID NO: 2 and residues 21-48 of SEQ ID NO: 4 comprise the SPLAG domain.

3-OST-1 and all known NST species possess a homologous

carboxy terminal sulfotransferase (ST) domain of ~260 amino acids (residues 53-311 of SEQ ID NO: 2 and residues 49-307 of SEQ ID NO: 4) that exhibits homology to all known sulfotransferases and which includes the minimal fragment necessary for sulfation activity. (See page 12, lines 7-10.)

Thus, Applicants teach that residues 53-311 of SEQ ID NO: 2 and residues 49-307 of SEQ ID NO: 4 comprise the sulfotransferase domain, which converts a GlcA→GlcNS ±6S polysaccharide sequence to the sequence to GlcA→GlcNS 3S ±6S.

Figure 2 shows a sequence alignment of the ST domains of the sulfotransferases NST-1 (SEQ ID NO: 13), NST-2 (SEQ ID NO: 14), OST-1, OST-2, OST-3A/B, and OST-4. Within this region is a conserved sequence (at residues 260-269 of SEQ ID NO: 2, and 256-265 of SEQ ID NO: 4) which is a presumptive cysteine-bridged peptide loop thought to be involved in heparan sulfate substrate specificity. (See page 12, lines 11-15.)

Thus, Applicants teach that residues 260-269 of SEQ ID NO: 2, and 256-265 of SEQ ID NO: 4 comprise the cysteine-bridged peptide loop.

This cysteine-bridged peptide loop is part of the larger HS-binding domain (residues 250-276 of SEQ ID NO: 2 and 246-272 of SEQ ID NO: 4). A conserved lysine residue (residue 68 of SEQ ID NO: 2, and 64 of SEQ ID NO: 4) is presumptively catalytic. (See page 12, lines 15-17.)

Thus, Applicants teach that residues 250-276 of SEQ ID NO: 2 and 246-272 of SEQ ID NO: 4 comprise the HS-binding loop.

In view of the foregoing, Applicants submit that new claims 61-76 comply with the requirements of 35 U.S.C. §112, first paragraph.

*Claims 1-12 -- 35 U.S.C. §112, first paragraph*

Claims 1-12 were rejected under 35 U.S.C. §112, first paragraph, as failing to meet the enablement requirement. In particular, the Office Action suggests that the specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention.

The Office Actions states that the specification is enabling for the following:

- (i) an isolated nucleic acid that encodes a human or mouse 3-OST-1 protein;
- (ii) an isolated nucleic acid comprising the nucleotide sequence of SEQ ID NO 1 or SEQ ID NO 3;
- (iii) an isolated nucleic acid that encodes a mature murine or human 3-OST-1 protein;
- (iv) an isolated nucleic acid that encodes murine or human 3-OST-1 protein disclosed in SEQ ID NO 2 and SEQ ID NO 4 respectively;
- (v) an isolated nucleic acid that encodes a 3-O-sulfotransferase domain of the human or mouse 3-OST-1 protein wherein the domain consists of residues 53-311 of SEQ ID NO 2 or of residue 49-307 of SEQ ID NO 4;
- (vi) an isolated nucleic acid comprising at least 16 consecutive nucleotides of SEQ ID NO 2 or SEQ ID NO 4, and
- (vii) an isolated host cell selected from the group consisting of: bacterial cells, yeast cells, insect cells, and mammalian cells, wherein the mammalian cells are selected from the group consisting of: COS-7 cells, CHO, murine primary cardiac microvasculature endothelial cells, murine mast cell line C57.1, human primary endothelial or umbilical vein, F9 embryonal carcinoma cells, rat fat pad endothelial cells, and L cells, wherein the host cell comprises the nucleic acid. (See Paper No. 10, page 6, paragraph 7.)

New claims 61-76 are directed to the subject matter identified in the Office Action as properly enabled. Accordingly, Applicants submit that the rejection under 35 U.S.C. §112, first paragraph, should not be maintained against new claims 61-76.

**Rejections Under 35 U.S.C. §112, Second Paragraph**

*Claims 1-12 and 29-32 - 112, 2<sup>nd</sup> paragraph*

Claims 1-12 and 29-32 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. Claims 1-12 and 29-32 are cancelled by the present amendment, rendering the rejections under 35 U.S.C. §112, second paragraph moot.

The Office Action further suggests that claims 1-12 are indefinite because they recited inventions not elected for prosecution. Following entry of the present amendment, claims 1-12 and 29-32 are cancelled, and claims 13-28 and 33-60 are withdrawn. Thus, none of the claims presented for consideration recite the non-elected subject matter. Accordingly, Applicants submit that new claims 61-76 satisfy the requirements of 35 U.S.C. §112, second paragraph.

*Claims 2-12 and 29-32 -- 35 U.S.C. §112, second paragraph*

Claims 2-12 and 29-32 were rejected as being indefinite 35 U.S.C. §112, second paragraph. Claim 2-12 and 29-32 are cancelled by the present amendment, rendering the rejections under 35 U.S.C. §112, first paragraph moot. Applicants submit that new claims 61-76 satisfy the requirements of 35 U.S.C. § 112, second paragraph.

**Rejections Under 35 U.S.C. §102**

Claim 7 was rejected under 35 U.S.C. §102(b) as being anticipated by Marra et al., Est Database Accession No. W62484, Jun. 1996 (herein "Marra 1"), P. Phillipsen et al., Sequence 906, Pat. No. 6,239,264 (herein "Phillipsen"), Marra et al., Est Database Accession No. AA041885, Sep. 1996, (herein "Marra 2"), and Hillier et al. Est Database Accession No. AA460705, Jun. 1996 (herein "Hillier"). Claim 7 has been cancelled, rendering these §102(b) rejections moot.

### SUMMARY

Claims 1-60 were pending in the Application. Claims 1-12 and 29-32 are cancelled, claims 13-28 and 33-60 are withdrawn, and new claims 61-76 are added by the present Amendment. Applicants respectfully submit that no new matter is introduced.

Applicants request that the Examiner reconsider the application and claims in light of the foregoing Amendment and Response, and respectfully submit that new claims 61-76 are in condition for allowance.

A petition and fee for a three-month Extension of Time for Response is submitted herewith. Applicants believes that no additional fees are necessitated by the present Amendment. However, in the event that any additional fees are due, the Commissioner is hereby authorized to charge any such fees to Attorney's Deposit Account No. 20-0531.

Respectfully submitted,

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